Notice of Allowability	Application No.	Applicant(s)	
	09/854,356	CHEEVER ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Response of 10/3/07*.

2. ☒ The allowed claim(s) is/are *113, 116-125, 146-156 (renumbered as Claims 1-22)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

DETAILED ACTION

1. Claims 113, 116-125 and 146-156 are all the pending claims for this application.

2. The amendment of Claims 113 and 116 in the Response of 10/3/07 has been considered and entered.

3. Claims 113, 116-125 and 146-156 are all the claims under examination

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

4. The rejection of Claims 113 and 117-125 for the recitation "where said SEQ ID NO: 6 is administered" in Claim 113, and Claims 116 and 146-156 are indefinite for the recitation "where said SEQ ID NO: 7 is administered" in Claim 116 is withdrawn.

Applicants' telephone instructions of 12/7/07 to amend Claims 113 and 116 to replace the respective phrases with "and where said polypeptide is administered" (see Examiner's Amendment below), obviates the rejection.

Applicants' comments on pp.7-9 of the Response of 10/3/07 are acknowledged.

35 USC § 112-first paragraph

Written Description

5. The rejection of Claims 113, 116-125 and 146-156 under 35 U.S.C. 112, first paragraph, in lacking written description support for generic claims, 113 and 116, reciting "comprising" language that reads on any polypeptide having within its amino acid sequence a region consisting of either SEQ ID NO:6 or 7 is withdrawn.

Claims 113 and 116 now recite that a polypeptide comprising SEQ ID NO: 6 (or SEQ ID NO:7) is administered (See Examiner's Amendment below). The claims no longer read on a literal SEQ ID NO: being administered to a subject.

Further, Applicants allegations on pp. 6-7 of the Response of 10/3/07 have been considered and are found persuasive. Applicants allege the specification discloses:

a) HER2 proteins for: 1) the full length Her-2/neu protein (SEQ ID NO:1), 2) the Her-2/neu fusion protein comprising SEQ ID NO: 6 (919 amino acid residues; the extracellular domain (ECD) and the phosphorylation domain (PD), 3) the Her-2/neu fusion protein of SEQ ID NO:7 (712 amino acid residues; the extracellular domain (ECD) and a preferred portion of the phosphorylation domain(ΔPD) of the human HER-2/neu protein (SEQ ID NO:7), 4) rat HER-2 (SEQ ID NOS: 2 and 8), 5) mouse HER2 (SEQ ID NO:14), and 6) ECD-ICD and ECD-PD constructs (pp. 13 and 19); LAB

b) multiple polypeptides comprising SEQ ID NO:6 or 7 fused to unrelated immunological peptides (pp. 22-23) and in Example 9, a mouse ECD-PD construct fused to Ra12 fragment of M. tuberculosis.

Enablement

6. The rejection of Claims 113, 155, 116 and 156 under 35 U.S.C. 112, first paragraph, in lacking enablement for using the method to elicit or enhance an immune response in a human is withdrawn.

Claims 113 and 116 now recite that a polypeptide comprising SEQ ID NO: 6 (or SEQ ID NO:7) is administered (See Examiner's Amendment below). The claims no longer read on a literal SEQ ID NO: being administered to a subject.

Further, Applicants' allegations on pp. 9-14 of the Response of 10/3/07 regarding the Kurebayashi reference, the Limentani Abstract and the 1.132 Declaration of Dr. Jamila Louahed are found persuasive.

On pp. 9-11, Applicants assert that Kurebayashi (Exp. Opin. Pharmacother. 1(4):603-614 (2000); cited in the IDS of 6/13/07) is cited to describe the state of art in immunotherapeutics for HER2-expressing breast cancer with respect to the recognition of naturally occurring HER2 antibodies in breast cancer patients. Applicants allege that even though Kurebayashi specifically states that it is unknown whether immunity to HER2 predicts improved survival, this conclusion ~~is~~ as LAB taken alone is not evidence of non-enablement. Applicants point out that the specification teaches a HER-2/neu fusion protein comprising SEQ ID NO:6 or 7 can stimulate T cell proliferation and cytotoxicity and induce B cells to produce an antibody.

Applicants have now provided a copy of Limentani Poster Abstract describing treating Stage II and Stage III Her2+ breast cancer in human patients with the 919 amino acid sequence of SEQ ID NO:6 in combination with adjuvant AS15.

On pp. 12-14, Applicants have addressed the Examiner's concerns regarding the apparent discrepancy in the meaning of the laboratory names and terms used in the Poster Abstract, Limentani reference and the Declaration of Dr. Louahed for the instant claimed polypeptides comprising SEQ ID NOS: 6 or 7.

Applicants aver on p. 13:

" The specification at page 7 states that an ECD/ICD polypeptide comprises the extracellular domain and the intracellular domain or fragments thereof but does not contain a substantial portion (if any) of the transmembrane. An ECD/PD polypeptide is described (still on page 7) as polypeptides comprising the extracellular domain and the phosphorylation domain but not containing a substantial portion (if any) of the transmembrane domain. As noted on page 7 (e.g., in first full paragraph), the PD is found within the ICD, thus the PD is a fragment of the ICD. From the specification as a whole, it is clear that ECD/PD polypeptides are a subset of ECD/ICD polypeptides. SEQ ID NO:6 is a specific ECD/PD polypeptide, and is also an example of a polypeptide consisting of the ECD and a fragment of the ICD (where the fragment is the PD)."

Applicants aver on p. 13:

"The Limentani Abstract describes a recombinant HER2 protein that included the extra-cellular domain and part of the intra-cellular domain of HER2, and refers to this as an ECD/ICD polypeptide."

Applicants aver on p. 14:

"However, any "contradictions" between the terminology used in the Limantani references and that of the specification is specifically addressed by Dr. Louahed's factual declaration. Dr. Louahed states (para 7) that the recombinant HER2 protein used in the studies described in the Limentani references was the 919 amino acid sequence of SEQ ID NO: 6."

EXAMINER'S AMENDMENT

7. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Virginia Campen on 12/7/07.

The application has been amended as follows:

113. (Currently amended) A method for eliciting or enhancing an immune response to HER-2/neu protein in a warm-blooded animal, the method comprising administering to said warm-blooded animal a composition comprising a polypeptide, where said polypeptide ~~comprising the amino acid of~~ comprises SEQ ID NO:6, and where said ~~SEQ ID NO:6~~ polypeptide is administered in an amount effective to elicit or enhance the immune response to HER-2/~~Neu~~ neu, and wherein the response to HER-2/neu is elicited or enhanced in said animal.

116. (Currently amended) A method for eliciting or enhancing an immune response to HER-2/neu protein in a warm-blooded animal, the method comprising administering to said warm-blooded animal a composition comprising a polypeptide, where said polypeptide ~~comprising the amino acid of~~ comprises SEQ ID NO:7, and where said ~~SEQ ID NO:7~~ polypeptide is administered in an amount effective to elicit or enhance the immune response to HER-2/~~Neu~~ neu, and wherein the response to HER-2/neu is elicited or enhanced in said animal.

EXAMINER'S STATEMENT FOR REASONS FOR ALLOWANCE

8. The following is an examiner's statement of reasons for allowance:

Applicants have shown by a preponderance of the evidence that the administration of the Her-2/neu fusion polypeptide comprising SEQ ID NO:6 or 7 can elicit or enhance an

immune response in T and B cells and in human breast cancer patients given the polypeptide comprising SEQ ID NO:6.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

9. Claims 113, 116-125 and 146-156 are allowed and are renumbered as Claims 1-22.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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